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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/524,690

**Applicant(s)**

LOWE ET AL.

**Examiner**

TERRA C. GIBBS

**Art Unit**

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-37, 39, 41, 42 and 45-57 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-37, 39, 41, 42 and 45-57 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ ~~Notice of Informal Patent Application~~
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

This Office Action is a response to Applicant's Preliminary Amendment filed November 21, 2006.

Claims 38, 40, 43, and 44 have been canceled.

Claims 1-37, 39, 41, 42 and 45-57 are pending in the instant application.

Claims 1-37, 39, 41, 42 and 45-57 are subject to restriction under 35 U.S.C. 121 and 372 as detailed below:

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 39 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39 recites the limitation, "The method of claim 38". There is insufficient antecedent basis for this limitation in the claim because claim 38 has been canceled. Accordingly, claim 39 has not been included in the restriction requirement because the claim cannot be constructed into an appropriate Group since the claim is dependent on a canceled claim. Thus, the metes and bounds of claim 39 cannot be determined.

***Election/Restrictions***

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 3-5, drawn to a method for introducing into a subject a population of stem cells having partial or complete loss of function of a target gene, wherein the target gene encodes a host protein that is co-opted by a virus during viral infection.

Group II, claim 6, drawn to a method for introducing into a subject a population of stem cells having partial or complete loss of function of a target gene, wherein the target gene encodes a polypeptide of a Major Histocompatibility Complex.

Group III, claims 31 and 32, drawn to a non-human mammal comprising a population of stem cells comprising a nucleic acid construct encoding an shRNA, or progeny cells thereof, wherein the cells exhibit partial to complete loss of function of a target gene.

Group IV, claims 33 and 34, drawn to a composition formulated for administration to a human patient the composition comprising a) a stem cell comprising a nucleic acid construct encoding an shRNA, wherein the shRNA is complementary to at least a portion of a target gene, and wherein the cells exhibit partial to complete loss of function of a target gene, and (b) a pharmaceutically acceptable excipient.

Group V, claims 35-37, drawn to a method for identifying a gene that affects the sensitivity of tumor cells to a chemotherapeutic agent.

Group VI, claims 41 and 42, drawn to a method of administering a chemotherapeutic agent to a patient.

Group VII, claims 45-49, drawn to a method of determining a function of a gene or a method of determining the contribution of a gene to a condition.

Group VIII, claims 50-55, drawn to a method of engineering cells *ex vivo* so that the cells exhibit reduced expression of a gene product.

Group IX, claims 56 and 57, drawn to a method for introducing into a subject a

population of stem cells having partial or complete loss of function of a target gene, wherein the method comprises a) introducing a nucleic acid construct encoding an shRNA, and b) removing or inactivating the nucleic acid construct, wherein removing or inactivating the nucleic acid construct comprising introducing or activating Cre.

Claims 1, 2, and 7-30 links the inventions of Groups I and II. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claims, claims 1, 2, and 7-30. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

This application does not comply with the requirements of unity of invention (Rules 13.1, 13.2, and 13.3) for the following reasons:

Group I is directed to a method for introducing into a subject a population of stem cells having partial or complete loss of function of a target gene, wherein the target gene encodes a host protein that is co-opted by a virus during viral infection, said target gene encoding a host protein that is co-opted by a virus during viral infection is not

identified in any of the other Groups and thus clearly contains its own special technical feature.

Group II is directed to a method for introducing into a subject a population of stem cells having partial or complete loss of function of a target gene, wherein the target gene encodes a polypeptide of a Major Histocompatibility Complex, said target gene encoding a polypeptide of a Major Histocompatibility Complex is not identified in any of the other Groups and thus clearly contains its own special technical feature.

Group III is directed to a non-human mammal comprising a population of stem cells comprising a nucleic acid construct encoding an shRNA, or progeny cells thereof, wherein the cells exhibit partial to complete loss of function of a target gene, said non-human mammal is not identified in any of the other Groups and thus clearly contains its own special technical feature.

Group IV is directed to a composition formulated for administration to a human patient the composition comprising a) a stem cell comprising a nucleic acid construct encoding an shRNA, wherein the shRNA is complementary to at least a portion of a target gene, and wherein the cells exhibit partial to complete loss of function of a target gene, and (b) a pharmaceutically acceptable excipient, said composition and pharmaceutically acceptable excipient is not identified in any of the other Groups and thus clearly contains its own special technical feature.

Group V is directed to a method for identifying a gene that affects the sensitivity of tumor cells to a chemotherapeutic agent, said method is not identified in any of the other Groups and thus clearly contains its own special technical feature.

Group VI is directed to a method of administering a chemotherapeutic agent to a patient, said method is not identified in any of the other Groups and thus clearly contains its own special technical feature.

Group VII is directed to a method of determining a function of a gene or a method of determining the contribution of a gene to a condition, said method is not identified in any of the other Groups and thus clearly contains its own special technical feature.

Group VIII is directed to a method of engineering cells *ex vivo* so that the cells exhibit reduced expression of a gene product, said method is not identified in any of the other Groups and thus clearly contains its own special technical feature.

Group IX is directed to a method for introducing into a subject a population of stem cells having partial or complete loss of function of a target gene, wherein the method comprises a) introducing a nucleic acid construct encoding an shRNA, and b) removing or inactivating the nucleic acid construct, wherein removing or inactivating the nucleic acid construct comprising introducing or activating Cre, said method is not identified in any of the other Groups and thus clearly contains its own special technical feature.

The inventions listed as Groups I-IX do not relate to each other. The inventions do not possess a single general inventive concept under PCT Rule 13.1 because under PCT Rule 13.2, they lack the same or corresponding special technical feature for the following reasons: The special technical feature of one Group clearly has a different special technical feature that is not present in another Group. Thus, the inventions of

Groups I-IX do not share a common chemical core structure with each other.

Furthermore, the inventions listed as Groups I-IX do not possess a single general inventive concept under PCT Rule 13.1 because under PCT Rule 13.2, they lack the same or corresponding special technical feature for the following reasons: Groups I-IX do not avoid the prior art because a method for introducing into a subject a population of stem cells having partial or complete loss of function of a target gene was disclosed in the prior art of Paddison et al., in view of Lee et al., and Wianny et al. (all references have been made of record on the Information Disclosure Statement filed January 16, 2007).

Paddison et al. describe that the RNA interference effects of exogenously provided dsRNAs can be recapitulated in mammalian cells by the expression of single RNA molecules which fold into stable hairpin structures and transient transfection of plasmids encoding small hairpin RNAs (shRNAs) can achieve a near complete reduction in the levels of a specific protein in a cell. Paddison et al. also teach mouse embryonic stem cells transfected with dsRNAs. Lee et al. describe short hairpin type of dsRNAs significantly induce RNAi-mediated gene silencing in the cytoplasm of human cells. Wianny et al. describe the specific interference of gene function by double-stranded RNA in early mouse development. Thus, it would have been obvious to the practitioner in the art at the time of filing of the instant invention to devise a method for introducing into a subject, a population of stem cells having partial or complete loss of function of a target gene, using the mouse embryonic stem cells transfected with dsRNAs of Paddison et al. and the mice injected with dsRNA of Wianny et al. to study

development and gene regulation in normal and diseased cells. One of ordinary skill in the art would have been motivated to devise a method for introducing, into a subject, a population of stem cells having partial or complete loss of function of a target gene to treat disease such as lymphomas.

Therefore, Groups I-IX lack unity because a method for introducing into a subject a population of stem cells having partial or complete loss of function of a target gene was known in the prior art. Therefore, there is no common special technical feature which exists between the aforementioned Groups.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

- (a) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;
- (b) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);
- (c) the prior art applicable to one invention would not likely be applicable to another invention;
- (d) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

**Applicant is advised that the reply to this requirement to be complete must include (i) an election of an invention to be examined even though the requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.**

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(l).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758. The examiner can normally be reached from 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

September 28, 2010

/Terra Cotta Gibbs/